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A REVIEW STUDY ON RAMAN SPECTROMETER AND ITS APPLICATION IN PHARMACEUTICAL INDUSTRIES

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ABSTRACT

Raman spectroscopy is a vibrational spectroscopic approach for easily interpreting and structurally identifying tiny quantities of compounds, solids, liquids, and gases based on their distinct vibrational properties. The purpose of this study is to provide an overview of Raman spectrometers in the field of pharmaceutical analysis. How has the development of the Raman spectrometer aided the pharmaceutical industry? Detection of a wide range of placebos, medications, substances, and their structures. How do they feel about the characteristics following the reaction?

This spectroscopic method is used for qualitative and quantitative analysis of trace amounts of counterfeit drugs and other illegal substances on various matrices in a non-destructive manner without extensive sample preparation. This paper also describes Raman spectroscopy, its types, and its major applications.

This study also includes a brief overview of Raman spectroscopy, including theoretical approaches, evolution, and numerous techniques, which are utilized for various studies. The field of light collecting and suitable source selection for the application is at the heart of the Raman spectrometer.

How may the source and its accompanying optics be beneficial for the application in question? The report also proposes research to improve and develop the flexible low-cost Raman in the pharmaceutical industry, particularly for illegal substance analysis. The Raman spectroscopy method is based on the inelastic scattering of light by materials. Light scatters in two different ways: elastically and in elastically. Where the wavelengths of scattered light are the same and different. By detecting that one can offer the structural information about the samples, the wavelength shift describes the energy transfer from one incoming photon to the molecules of the sample.

KEYWORDS: Raman Spectrometer, Pharmaceutical & Illicit Drug

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Original Article

1. INTRODUCTION

Since science's growth is in full swing, there have been numerous discoveries to satisfy the need for knowledge. Invention in a variety of disciplines is a prime illustration of this. Not just the earth, but even the oceans and the limitless universe are being explored. Nothing is left neglected, whether it be matter or energy. The field of spectroscopy is used to search for information about things that have aided innovators.

Spectroscopic methods may be used to study the behavior of matter, its interactions, and its underlying science. Almost all occurrences involving matter can be investigated using spectroscopic methods. The Raman spectrometer is a flexible spectroscopic technique for analyzing matter's intrinsic structure, atomic behavior, and electron molecule orientation.

Raman spectroscopy is a useful tool for studying the structure and behavior of molecular materials and condensed matter. It is based on the inelastic scattering of monochromatic light, which is generally visible, near infrared, or near ultraviolet in wavelength.

It's a type of vibrational spectroscopy that enables simple structural identification and interpretation of tiny quantities of compounds based on their distinctive vibrational properties (fingerprints). When monochromatic light is focused on a sample, a tiny proportion (1/103) of the incoming light is transformed into scattered radiations, and a small fraction (1/103) of the dispersed radiation is scattered inelastically. There are two types of dispersed light: elastic and inelastically scattered light. Elastically scattered light has a wavelength that matches that of the incident radiation, whereas inelastic scattering has a wavelength that differs from that of the incident radiation. Inelastic scattering occurs in just (1/106) photons. [1,2]

The scattering is measured in Raman shift, which may be computed using the following formula:

$$\Delta\nu = [1/\lambda_0 - 1/\lambda_1]$$

$$\Delta\nu\ (cm^{-1}) = [1/\lambda_{0\ (nm)} - 1/\lambda_{1(nm)}] \times [10^7 nm/cm] \quad \text{(Eq.1)}$$

2. THEORY OF RAMAN SCATTERING

The dual behavior of particle and wave in nature is demonstrated by light. Raman Scattering may be defined in two ways: a) Quantum and b) Physical. It viewed light as a particle, as opposed to b) Classical, which treats light as a wave.

2.1 Quantum Approach to Find the Intensity of Raman Spectra

The interacting molecule in the material system is treated quantum mechanically in the quantum mechanical approach of light-scattering events, while the electromagnetic radiation is still treated conventionally. We take into account the incident's electric and magnetic fields.

To compute the characteristics of the perturbed system, consider electromagnetic radiation as generating perturbations of the molecule's states, then employ quantum mechanics methods. The allowed transitions between states of the molecule when perturbed by incoming radiation, as well as the frequency-dependent multiple transition moments, will be of special interest. By treating such frequency-dependent multiple transition moments as classical multiple sources of electromagnetic radiation, the characteristics of the dispersed radiation may be established. Placzek initially utilized Raman scattering in 1934 [6,7], and it works as follows:

$$I_R = \frac{(2\hat{}4*\pi\hat{}3)}{45*32*c^2} * \frac{[\ h\ I_L\ (\nu_0-\nu)^4\ ]}{\mu\ \nu\ (1-\ e^{-h\nu/kT})} * [45(A'_a)^2+(Y'_a)^2\ ]$$

(Figure 1 Intensity of Raman Spectra- Eq. 2)

where**:**

c = speed of light

h= plank constant

I_L= excitation intensity

N= number of scattering molecule

ν= Molecular vibration frequency

ν_0= laser excitation frequency Hz

μ= reduced mass of the vibrating atom

k= Boltzmann's constant

T= absolute temperature

A'_a= mean value invariant of the polarizability tensor

Y'_a= anisotropy of the invariant of the polarizability tensor

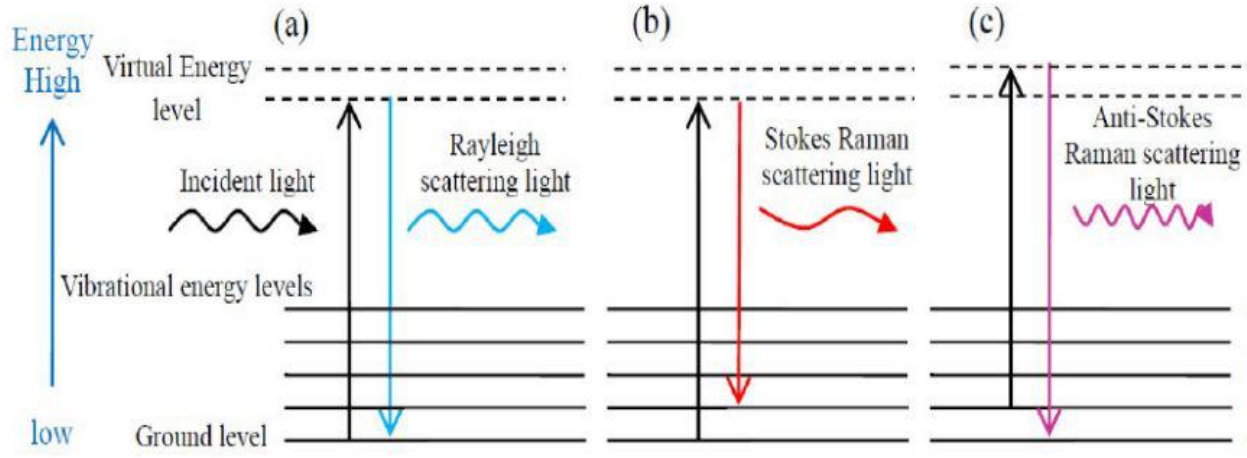

Figure 2: Diagram of a) Rayleigh Scattering, b) Stokes Scattering, c) Anti-Stokes Scattering.

2.2 Classical Approach to Calculate the Intensity of Raman Spectra

When light scatters from a molecule, the incoming electromagnetic wave's time-dependent electric field component bends the molecule's electron cloud, causing an electric dipole moment. Due to the significantly smaller size of the molecule compared to the usual wavelength of Raman excitation in the visible portion of the electromagnetic spectrum (400–700 nm), the molecule perceives the incoming electromagnetic wave as an oscillating electric field. The extent of the electron cloud distortion depends on its polarizability, α. In a classical description, the induced electric dipole moment, P, can be defined as follows:

$$P = \alpha E = \alpha E_0 \cos(2\pi\nu_0 t), \quad \text{(Eq: 3)}$$

The electric field component of the entering electromagnetic wave has an amplitude of E0 and a frequency of ν0. The nuclear displacement q in the simplest instance of a diatomic molecule (harmonic oscillator) vibrating at frequency m is:

$$q = q_0 \cos(2\pi\nu_m t) \quad \text{(Eq: 4)}$$

Where q0 is the molecular vibration's amplitude (maximum displacement). A linear function of q (linear term of the Taylor series) can be used to approximate for tiny amplitudes of molecular vibration:

$$\alpha = \alpha 0 + (\delta\alpha/\delta q)0 * q + \ldots \ldots \text{(Eq: 5)}$$

where $\alpha 0$ is the polarizability at the equilibrium position and ($\delta\alpha/\delta q$)0 is the derivative of α with respect to the change in q, evaluated at the equilibrium position. The expression for the induced dipole moment can then be written as follows:

$$P = \alpha 0 E0 \cos(2\pi\nu 0t) + (1/2)*(\delta\alpha/\delta q)0*q0*E0\{\cos[2\pi(\nu 0 + \nu m)t] + \cos[2\pi(\nu 0 - \nu m)t]\} \ldots \ldots \text{(Eq: 6)}$$

The three contributions to the scattered radiation appear as separate terms with $\nu 0$ for the Rayleigh scattering case, $\nu 0 - \nu m$, for the Stokes Raman scattering case, and $\nu 0 + \nu m$ for the anti-Stokes Raman scattering case. The expression implies that if the derivative ($\delta\alpha/\delta q$)0 is zero, or in other words, if the polarizability does not change during a vibration, then it is not Raman active. If we consider an oscillating induced dipole to be the source of radiation, the resulting intensity of the Stokes Raman scattered light can be described with the following expression **[**5**]**

$$I \propto (\delta\alpha/\delta q)_0 \wedge 2 * I0*(\nu 0 - \nu m)\wedge 4 \ldots \ldots \text{(Eq: 7)}$$

Therefore, the intensity depends on the derivative of the polarizability, the intensity of the incident radiation $I0$, and the frequency of the scattered light. Note the fourth-power dependence of the signal intensity on the frequency of the scattered radiation (Figure **2**). This frequency dependence, however, is not valid if $\nu 0$ is close to the frequency of an electronic transition of the molecule. In this case, significantly higher Raman scattering intensities (resonance Raman scattering) are observed.

3. EVOLUTION OF RAMAN SPECTROSCOPY

The Mercury arc lamp served as the light source, the telescope served as the collection optics, and photographic plates served as the detector in the first Raman spectrometer. Gradually, as technology progressed, advancements in source, collecting optics, filter assembly, and detectors, ranging from stenographic plates to PMTs and finally CCD, significantly altered the Raman era. Until the 1960s, a mercury arc lamp was employed as a light source [10,11]. In the late 1960s, laser sources were accessible, and the mercury lamp was fully replaced[11]. These laser sources provide a consistent and powerful beam of light. In a Raman spectrometer, near-infrared (IR) diode lasers can be utilized as the light source[12]. Short-wavelength sources like argon-ion and krypton-ion lasers can induce considerable fluorescence and sample photo-decomposition. Long-wavelength sources, such as diode or Nd: YAG lasers, may, on the other hand, be operated at considerably greater power without producing photo-decomposition of the material and, in most circumstances, remove or decrease fluorescence[11].To isolate a single laser beam, band-pass filters are utilized.

In dispersive instruments, the most common combination of notch filter and high-quality grating Monochromator is employed. Double, triple, or even quadruple grating To distinguish relatively weak Raman lines from strong Rayleigh radiation, monochromators, super notch filters, rejection filters, holographic notch or edge filters, and holographic filters are employed.[10,11,13]. Early versions of dispersive Raman spectrometers employed thermo electrically cooled photomultiplier tubes and photo-diode array detectors[10]. More sensitive charge transfer devices (CTDs) such as charge-coupled devices (CCDs) and charge-injection devices have replaced these detectors due to advances in instrumentation and technology (CIDs). These devices serve as detectors and are arranged in arrays. Photo-site transforms incoming optical signals into a charge, which is integrated and transmitted to readout devices in CTD arrays[11]. With laser wavelengths less than 1 m, multichannel CCD detectors are utilized, whereas single element narrow band-gap semiconductor Ge or InGaAs

detectors are employed with laser wavelengths higher than 1 m [11,13]. In the late 1980s, commercial Fourier Transform-Raman spectrometers (FT-Raman) were created to increase detection system capacity by overcoming the limits of CCD and other detectors for working in the near-IR region utilizing a 1064 nm laser excitation[13]. A Michelson interferometer and a continuous-wave laser, such as Nd–YAG, produce radiation at 1064 nm in FT-Raman spectrometers.

4. INSTRUMENTATION OF RAMAN SPECTROSCOPY

Raman Instrumentation is responsible for component selection and validation. A monochromatic source, collection optics, and a spectrometer make up a standard Raman Spectrometer. Prof. CV. Raman created the very first Raman spectrometer in 1928. [2]The source was a mercury lamp, the collection optics was a telescope, and the detector was photographic plates. With the passage of time and technological advancements, the Raman Instrumentation has seen a significant transformation. Since the year 1960, the progress of the laser has been in full swing, with detectors such as CCDs enhancing its performance and Raman Microscopy giving greater spatial resolutions with the addition of appropriate objectives.

The collection and detection of Raman scattering geometry is normally categorized in two modes [20]. a) Right angle scattering collection mode, b) Back scattering collection mode

4.1. Right Angle scattering Collection Geometry (Figure.3)

In this collection mode, the collecting optics is positioned at a right angle to the incoming beam and gathers scattered light from the sample before focusing it on the spectrograph. Optical filters are put between the spectrograph and the collection optics to achieve the desired wavelength of light.

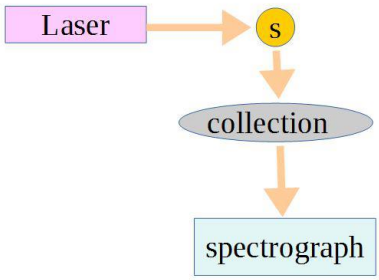

Figure 3: Right Angle Scattering Collection.

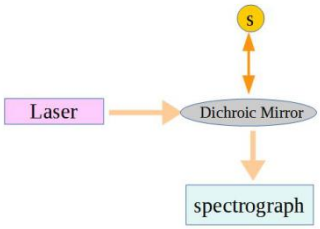

Figure 4: Back Scattering Collection.

4.2. Back Scattering Collection Geometry (Figure. 4)

Back scattering collection geometry occurs when scattered light is collected from the same direction as the incident beam, i.e. 180° from the incident beam or 135° from the incident beam. The incident and collected rays are separated using a

dichroic filter in this technique of collection, and dispersed light is focused on the spectrograph.

Advantage of Back Scattering over Right Angle Scattering

The back scattering collection geometry (135° or 180°) is preferable than the right angle scattering collection geometry [20]. They can acquire Raman spectra on tiny samples even at low temperatures since changing samples and going to the next analysis is easier. Raman scattering and UV-Vis absorption can both be measured at the same time. Self-absorption correction is simple to do for strongly colored solutions.

5. RAMAN SPECTROSCOPY: VARIANTS AND EARLIER ANALYSIS

Conventional Raman spectroscopy and enhanced Raman spectroscopy are the two main types of Raman spectroscopy. The most common reason for creating variations is to improve sensitivity (e.g., surface-enhanced Raman), spatial resolution (Raman microscopy), or gather highly particular data (resonance Raman). A basic experimental set up is constructed in the traditional Raman spectroscopy approach, in which the source impinges on the sample and the scattered light is collected by a collection optics, generally a lens. The captured light is then filtered to get the Raman Scattering. Enhancement techniques are employed in enhanced Raman Spectroscopy to boost the intensity of scattered light. Which are as follows:

5.1 Spontaneous (or Far-Field) Raman Spectroscopy

Raman spectroscopy approaches based on scattering utilizing standard far-field optics are referred to as spontaneous Raman spectroscopy or normal Raman spectroscopy. Excitation-detection geometries, integration with other methods, use of customized optics, and particular excitation wavelength selection for resonance amplification are all examples of variations of standard Raman spectroscopy.

A) Resonance Raman Spectroscopy (RRS):

The variable source of light is used to tailor the excitation wavelength to an electronic transition of the molecule under test, resulting in substantially increased vibrational modes associated with the excited electronic state. It may boost the intensity of Raman lines by up to 102-104 times over a standard one. This is especially beneficial for biochemical or process chemical samples containing a variety of chemicals. In such a sample, one can choose a source that absorbs in the provided components, resulting in a Raman intensity peak. [8]

B) Spatially offset Raman Spectroscopy (SORS)

By spatially offsetting the detection and excitation fibers, SORS captures the Raman signal from deeper regions in the tissue. It makes use of a detecting fiber that is surrounded by illuminating fibers.

C) Raman optical activity (ROA)

It uses a tiny variation in the intensity of Raman scattering from chiral compounds to measure vibrational optical activity. [19]

5.2 Enhanced (or Near-Field) Raman Spectroscopy

Local electric-field augmentation through optical near-field effects is used to improve Raman scattering (e.g. localized surface plasmons).

A) Surface-Enhanced Raman Spectroscopy (SERS): The low signal strength of RS is definitely a big drawback. To create electromagnetic and chemical amplification, one alternative to coherent signal amplification is to employ processes happening near a metal surface, such as metal nanoparticles. Nanoparticles create a localized surface plasmon resonance in the presence of an incoming electromagnetic field, which improves illumination at the pump frequency and the Raman signal at the Stokes frequency. It may boost the intensity of Raman lines by 102-106 times over the standard method. [9]

B) Surface-Enhanced Resonance Raman Spectroscopy (SERRS)

A combo of SERS and resonance Raman spectroscopy that employs proximity to a surface to boost Raman intensity and match the excitation wavelength to the molecule's maximum absorption. [8,9]

C) Tip-enhanced Raman spectroscopy (TERS)

TERS enhances the Raman signals of molecules in its proximity using a metallic (typically silver/gold-coated AFM or STM) tip. The spatial resolution is almost equal to the tip apex size (20–30 nm). TERS has been demonstrated to exhibit sensitivity down to the single molecule level, suggesting that it might be useful in bio-analysis[14].

5.3 Non-Linear Raman Spectroscopy

Non-linear optical effects are used to boost Raman signals, which are generally accomplished by combining two or more wavelengths generated by spatially and temporally synchronized pulsed lasers.

A) Coherent Anti-Stokes Raman Spectroscopy (CARS)

Coherent anti-stoke Raman scattering spectroscopy is utilized to improve the Raman signal in nonlinear Raman spectroscopy [15]. CARS is an anti-stoke frequency approach because it employs coherent laser beams to create a signal with a frequency that is higher than the excitation frequency. Duncan et al are credited with creating the first CARS structure in 1982 [16].

B) Hyper Raman Scattering (HR) Scattering

The vibrational modes interact with the second harmonic of the excitation source in this nonlinear Raman spectroscopy. It usually necessitates the use of a very powerful laser. [17]

C) Stimulated Raman Scattering (SRS)

The incidence of two photons is the fundamental premise of this coherent phenomenon (pump and stoke). On the sample, the two laser beams coincide. The vibrational transition will be simulated when the frequency difference matches the chemical vibration frequency of a bond in the target molecule. [18]

6. Block Diagram of Proposed PC Based in-Line Raman Spectrometer

The Raman spectrometer and its variations have been investigated, and it has been discovered to be a highly strong and flexible spectrometer for qualitative and quantitative investigation. This study aims to identify a need and method for developing an in-line PC-based Raman Spectrometer for pharmaceutical sample analysis in the pharmaceutical industry.

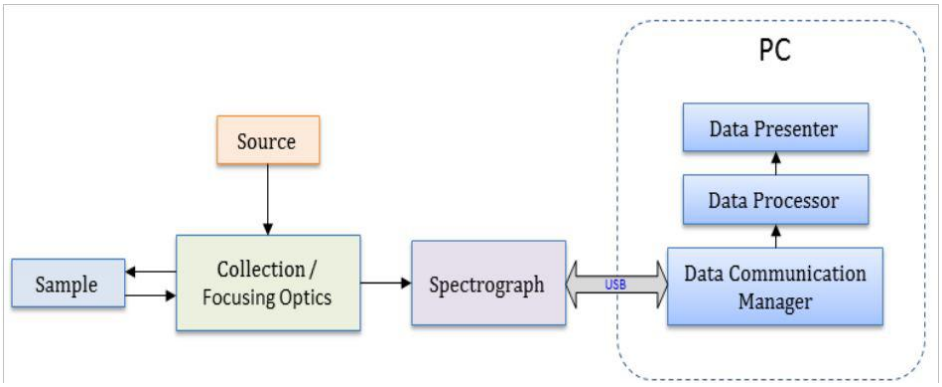

Figure 5: Block Diagram of Raman Spectrometer.

The suggested Raman spectrometer's design is depicted in the block diagram. It consists of a laser as a narrow light source, a high reflecting mirror to turn the laser beam in the required direction, a dichroic mirror to reflect the laser beam to sample through a focusing mirror that also acts as a collecting mirror for the scattered light, and a dichroic mirror to reflect the laser beam to sample through a focusing mirror that also acts as a collecting mirror for the scattered light.

After the light has been collected from the sample, it is sent to a filter to prevent any undesired scattering and then to a spectrograph to divide the light into its component wavelengths in order to determine the sample's fingerprint.

7. APPLICATIONS

For decades, a large number of articles have been published in the field of Raman spectroscopy for diverse activities and research applications. This review covers a few publications that explain current Raman Spectroscopy applications.

Using a Raman spectrometer, J. N. Willis et colleagues studied eight barbiturates (phenobarbital, pentobarbital, barbital, secobarbital, amobarbital, hexobarbital, butabarbital, and mephobarbital) and three sodium salt analogues. They discovered the Raman frequencies of carbonyl stretching and pyrimidine ring breathing vibrations and utilised them to identify all barbituric acids and their salts. [22]

Carter JC, et al. published a technique for quickly distinguishing between free base cocaine and cocaine hydrochloride. A substantial difference was detected between the spectra of cocaine hydrochloride and free base cocaine using a Surface enhanced Raman spectrometer with fibre optics probe. [23]

Ali EMA et al created a Raman spectrograph to detect Cocaine on human nails in 2008. On a 5-20 micrometer sample, this device employed a 50X objective lens with a 5 micrometer spot size. [24]

Using a portable Raman spectrometer, Hargreaves et al discovered the counterfeit drugs 3,4-Methylene Dioxymethamphetamine and Amphetamine Sulphate of unknown composition. It employed a 50mW 785nm laser and a cooled CCD as a detector. [25]

Weston RG et colleagues used a Raman Spectrometer to analyze 'Crystal Meth' (Sulphene and Methamphetamine). A 785nm laser was used to analyse the substance, and the intense band was identified at 703 cm-1 and 1004 cm-1. The peak is detected at 1208 cm-1, 826 cm-1, and 748 cm-1 in the detection of Crystal Meth with a concentration below 20%. [26]

Ali EMA et colleagues used a Raman spectrometer with an NIR diode laser of 49 mW to examine the effects of cocaine hydrochloride on natural fibers such as wool, silk, and cotton, as well as synthetic fibers such as polyesters. [27]

In 2011, Brunett AD et colleagues utilized a Raman spectrometer with a 785 nm laser to identify cocaine in color solutions. Because green color solutions had higher fluorescence, a 1064nm laser was used to detect cocaine in 0.5-10 percent W/V solutions, with peaks at 1730 cm-1, 1003 cm-1, and 1603 cm-1[28]. SERS method was utilized by Rana V et al to detect trace amounts of morphine and cocaine hydrochloride in their base form. A 785nm laser with a power of 100mW and a 633mW laser with a power of 30mW were used to obtain spectra from 2uL drugs[29].

Raman microscopy is used for detecting the drugs of abuse, metabolites, degradation products, and common cutting agents (allobarbital, amobarbital, barbital, phenobarbital, pentobarbital, secobarbital, chlordiazepoxide, diazepam, flunitrazepam, nitrazepam, cannabidiol, cannabinol, cocaine, ecgonine, amphetamine sulfate, fenethylline, methylenedioxymethamphetamine (MDEA), methylenedioxymethamphetamine (MDMA), methamphetamine, monoacetylmorphine, acetylcholine, heroin, morphine, papaverine, thebaine, caffeine, diphenhydramine, methaqualone, pemoline, procaine) using 532 nm laser. The substance under examination was trapped between glass plates for the experiment. [30]

Raman spectroscopy studies are also used to assess the quantitative and identity of illicit drug and powder samples that have been combined with diluent and varied drug proportions have been established by systematic sampling. Quantitative drug and hydrogen level measurements are also carried out for intelligent reasons. [31]

A portable Raman spectrometer with a 785 nm laser as an excitation source was utilized to analyze solid samples of illegal drugs, placebos, and real drugs, as well as 44 samples of active pharmaceutical ingredients (API) with different concentration analyses. [32]

Lu Feng et al. employed a portable Raman spectrometer with a 785 nm laser excitation wavelength and chemometrics to achieve excellent sensitivity, specificity, and accuracy in detecting synthetic pharmaceuticals contaminated in herbal medications and on-the-spot preliminary screening of suspected counterfeit drugs. Thermoelectric cooled (TEC) linear charge-coupled device array of 2048 elements is used for measurements, providing great stability and low dark counts. [33]

The transmission Raman spectrometer is used to perform matrix effect assessments in the quantitative assessment of a drug substance (DS) and the systematic examination of a solid pharmaceutical formulation. The analysis tablets were made according to the experimental design, with varied drug particle sizes (DS). [34] Bhumika et al [35] performed a spectroscopic review of Raman and compared it to other methods in the pharmaceutical area.

For the examination of gelatin-encapsulated tablets, food in bubble wraps, and containers using a 785nm excitation point source, a specific type of analysis called spatially offset Raman spectroscopy is utilized. Cunningham et al. created an optical system that can detect the drug concentration in fluid in real time [36,37]. Initially, the system analyses for morphine, methadone, phenobarbital, promethazine, and mitoxantrone; however, the technology can also identify combinations of two substances more quickly[38].

Raman has the advantage of being able to analyse samples in watery or high moisture environments. Excipients, paracetamol, and carbamazepine were also analysed using a 785 nm laser of 500mW and an integration duration of 8 seconds in the application note of ocean optics[39]. With an excitation wavelength of 785nm and a diode laser producing a

beam with a power of 10mW, a Raman spectrometer is used to identify ocular medications. At a 25X/0.50 objective lens, source light was focussed with a lengthy working distance. In quartz cuvettes, samples were tested 10 times in a row with a 30 second exposure time[40].

After diagnosing the condition, the next step is to discover a medication that will cure it. Designing a medication involves numerous processes, including chemical synthesis from scratch, biotechnology, and computer-aided drug design, among others. The Raman spectrometer is also used for lead compound characterisation, raw material analysis, formulation development, and in-process checks during formulation production and characterization[41,42].

Ingredients in pharmaceuticals that are active Ibuprofen (amorphous and crystalline forms) is a non-steroidal anti-inflammatory drug [43]. Psychostimulant Propranolol, alprenolol, acebutolol, and atenolol (stereoisomers) [44], b-blockers Propranolol, alprenolol, acebutolol, and atenolol (stereoisomers) (Amphetamine and methamphetamine) [45] a-indomethacin and g-indomethacin (polymorphs) are non-steroidal anti-inflammatory drugs [46]. The Raman spectrometer is used to examine the raw materials. M.G. Orkoula, et al[47] utilised a Raman spectrometer and HPLC to evaluate the stability of lovastatin, a cholesterol-lowering drug used to treat high blood pressure and cardiovascular disease, in the presence of Gallic acid.

Bruker IFS 66 Spectrometer with FRA106 FT-Raman module[48] is used to evaluate sized drugs of abuse such Cocaine, Heroin, MDMA, Cannabis, and Amphetamine, while RDX and PETN [49] are also identified for forensic reasons.

The stability of a medicine is critical if it is to be utilised in unusual environments such as the Atlantic, space, or underwater. Raman has been shown to be highly effective for drug stability analysis[50]. The Raman Spectrometer is used to analyse pharmaceutical formulations for Acebutolol, Alprenolol, Atenolol, Propanolol [51], Acetaminophen, Phenylpropanolamine [52]. Hitoshi Tsuchihashi et al.[53] used FT-Raman to determine MDMA and its related chemicals.

Raman spectroscopy is used to determine the scattering characteristics of a material, with probing light given to and collected from the sample using a transmission geometry used in pharmaceutical analysis such as tablet, diagnostic straps, and others. [54]. The characteristics of pharmaceutical tablets, such as surface roughness, gloss, and temperature, are measured in real time using a Raman spectrometer[55].

Raman spectrometers had limited applicability in the early days due to the poor efficiency of normal Raman scattering and the spectrometer parts being expensive and unsuitable for on-site examination. Raman spectroscopy structural development and enhancement allowed it to transcend such constraints. Instruments that are both portable and affordable are now available. For certain substances, the Raman spectrum is employed as a fingerprinting technique. As a result, it may be utilized for qualitative and quantitative examination in vivo, in vitro, and in situ.

8. CONCLUSIONS

In the field of sample detection, the Raman has shown to be the more essential and flexible instrument in the last decade. It allowed for ease of use and quick detection of the sample, as well as simpler sample analysis. This device has become more efficient and smaller as technology in the electrical and optical fields has progressed. In the realm of forensic science, it has proved its relevance and reliability in the analysis of drugs of abuse and illegal substances. Surface enhanced Raman scattering (SRS), coherent anti-stoke Raman scattering (CARS), Tip enhanced Raman scattering (TERS), stimulated and resonance Raman spectroscopy, and other sophisticated Raman methods increased the intensity of scattering light, allowing

for a high S/N ratio. Despite the fact that Raman spectrometers have a low intensity of scattering light and a weaker single to detect, their flexibility makes them highly helpful and dependable. Advances in optics and detecting electronics will make the device quicker, smaller, more cost-effective, and more efficient in the future.

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